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THE OCCURRENCE OF ENTAMOEBA HISTOLYTICA WITH TISSUE LESIONS IN THE TESTIS AND EPIDIDYMIS IN CHRONIC DYSENTERY *

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Amebas associated with pathologic processes have been reported as occurring in nearly every organ of the body, with the exception of the parts named in the title of this paper. As Dobell has pointed out, a large number of these reports on pathogenic ameboid organisms observed in man are either mistaken identifications of nonpathogenic forms, or misinterpretations. This is particularly true of the ameboid organisms reported as having been found in the urinary tract, lungs, pleural and peritoneal cavities, skin, and in pus from abscesses in various portions of the body. Many of these reports are probably misinterpretations of epithelial, mesothelial or endothelial cells, atypical cell-forms derived from granulation tissue, or of degenerating flagellates or other organisms. The vague and imperfect descriptions of most of these reports give additional grounds for their rejection.

No positive proof exists at the present time that there is any species of ameba pathogenic to man other than Entamoeba histolytica (Loeschia histolytica). This organism is widely distributed throughout the world; and, with the evidence at hand, this is the only species responsible for any amebic pathologic condition in man. It is generally recognized now as the sole etiologic agent in amebic dysentery and the secondary complications of this infection, such as hepatic, hepatopulmonic, splenic and cerebral abscess. In all of these secondary conditions amebas have been repeatedly demonstrated that cannot be distinuished from those in the primary intestinal lesions. The same thing has also been claimed by various observers for the skin, blood and urine; but the evidence given in these cases is too incomplete to be convincing.

There is no literature more confused and perplexing from the zoological standpoint than that on the ameba. To Dobell we are much indebted for his attempts to unravel this synonymic tangle. He shows that the species pathogenic to man is preferably called Entamoeba histolytica and this appellation is accepted by most writers. On the

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other hand, Castellani prefers Schaudinn's term, Loeschia histolytica. Without going further into this discussion the writer accepts for this report the views of Dobell and his criteria for the recognition of this organism.

The case reported here is a product of the routine microscopic study of all the organs and tissues from the necropsies made in this laboratory.

Case History.—A Russian Hebrew, aged 33, a boilermaker, was admitted to the Medical Clinic (Dr. Hewlett) April 20, 1916. He had acquired syphilis at the age of 17, and had been treated by injections over a period of five years; he has had no symptoms of the disease since. Eleven years previously (1904-5) he was in China during the Russo-Japanese War, and contracted dysentery. He had at that time from 20 to 40 bloody stools daily, but without pain. Food did not affect the condition. After three months he went back to Russia, where he apparently recovered. He came to the United States in 1910, going first to Chicago, and then to Detroit. Eighteen months before admission his intestinal trouble had returned. He had about ten stools daily, small in amount and bloody; they were painless, but he has always had a feeling of soreness in the right lower quadrant. His appetite remained good; he never vomited; food had no effect on his diarrhea. He was treated for about five weeks in Harper Hospital without any improvement. Six months before admission the blood disappeared from the stools, and after that time he continued to have from 8 to 9 watery stools a day. He took treatment all the time without results. He had lost 32 pounds during the last six months. He had had night sweats during the last 3 weeks. He did not cough; he was never jaundiced. He was always thirsty, and he had to get up four times nightly to pass water. There were no other symptoms.

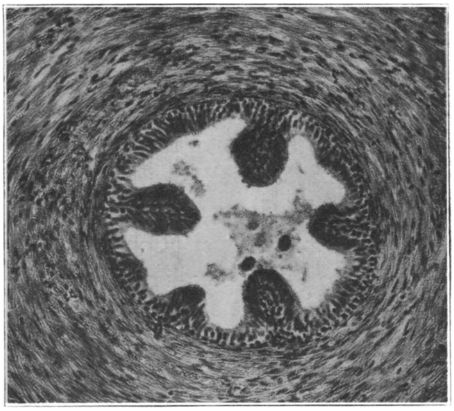

Fig. 1.—Section of upper portion of vas deferens, with small fibrin clot containing several amebas.

Physical examination revealed an anemic, underweight and undersized man, with numerous scars over the face and upper thorax, slight scarring at the angles of the lips, a brown, slightly indurated scar on the penis. There were tattoo marks on both arms. The cervical glands only were enlarged. The lower border of the liver was three finger breadths below the edge of the ribs in the nipple line. There was some tenderness on pressure over the liver. The spleen was not palpable. There was soreness in the right shoulder without limitation of movements or swelling. Examination of lungs was negative. The heart was over-active. The pulse rate was 120, regular and easily compressed. The temperature was 99.6 F.; respiration, 24. Roentgenologic report showed pleural thickening on the left side, with early tuberculosis of the right apex. A sclerosing glossitis (Dr. Wile). The blood contained 2,400,000 red blood cells, 16,000 white cells and 65% of hemoglobin. Urine examination was negative. The stools were soft and yellow, containing fat and meat fibers, occult blood, and many amebas of the type of *Entamoeba histolytica.*

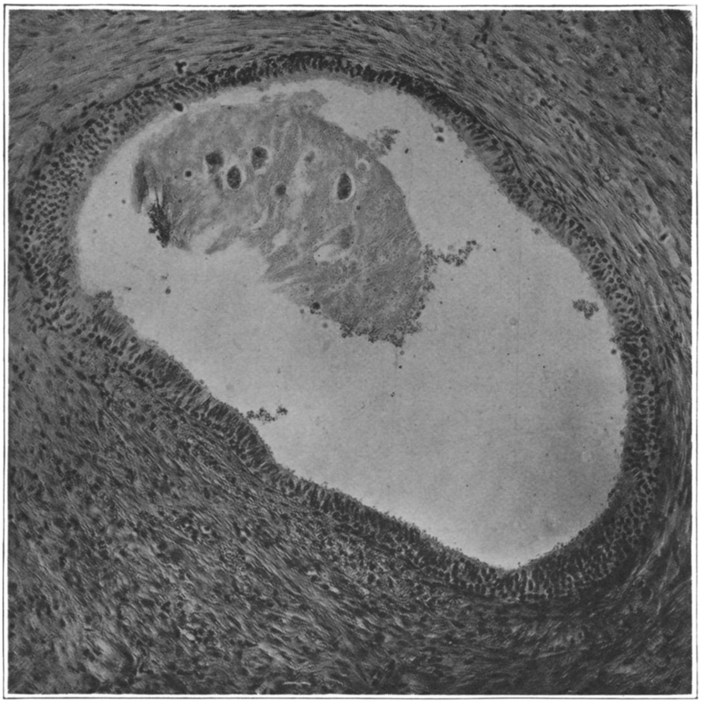

Fig. 2.—Section of tail of epididymis with fibrin clot containing a number of Entamoeba histolytica. The form of the amebas is made elliptical through contraction of the fibrin during fixation.

Clinical Diagnosis: Amebic dysentery; syphilis.

He was placed on emetin hydrochloride, bismuth, saline rectal irrigations, dilute hydrochloric acid and forced special milk diet. By May 8 the amebas had entirely disappeared from the stools, but his general condition was not improved. He ran a septic temperature, and the lower border of the liver descended, easily palpable and tender. He was, therefore, thought to have an amebic abscess of the liver and was referred to the Surgical Clinic (Dr. Darling) for operation. An exploratory laparotomy was performed May 9. No abscess was found at operation. Following the operation he developed pneumonia and died May 14. The stools remained free of amebas during the last 6 days.

Necropsy (Dr. Warthin) 2½ hours after death: The most important points of the protocol were:

Small, slender build; general nutrition poor; anemic; general edema; numerous scars over the face and trunk; pigmented scar on the penis; scars in angles of the lips; recent laparotomy wound in right hypochondrium, to the right of the median line, extending vertically, 10 cm. in length; abdomen below level of ribs; right arm tattooed with Russian characters; testicles small and firm; left epididymis enlarged; hydrocele and spermatocele on left side.

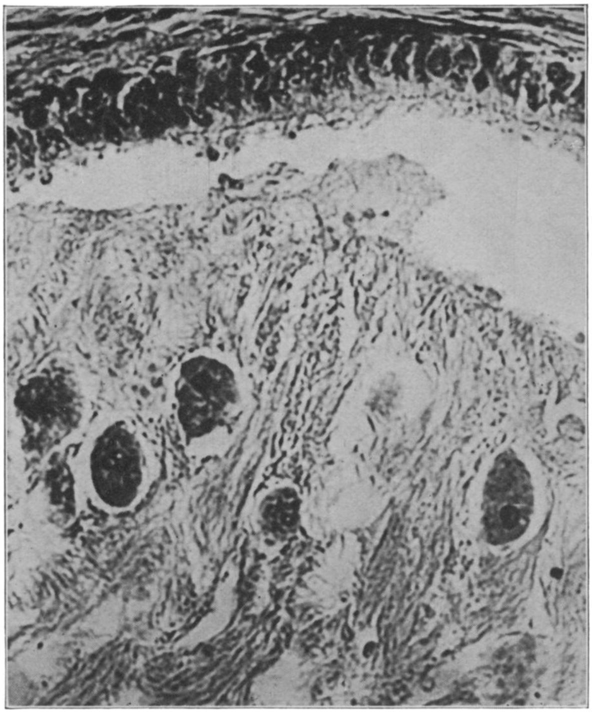

Fig. 3.—Higher power view of portion of clot containing Entamoeba histolytica, from tail of epididymis.

Upper portion of peritoneal cavity filled with a fibrinopurulent exudate; peritoneum cloudy and covered with exudate; surface of liver adherent to abdominal wall and to colon by fresh adhesions; heart small, "droplet heart"; large patch of sclerosis; orifices and valves negative; fatty change in muscle; lungs adherent by firm adhesions; left lower lobe airless, firm, on section presenting numerous small encapsulated abscesses; pressure forces many fibrinopurulent plugs from bronchioles and alveoli; unresolved croupous pneumonia;

spleen slightly larger than normal, firmer, purplish-red; on section, purplish-red, marked congestion, trabeculae not prominent, follicles small. No abscess.

Intestinal coils free throughout, with the exception of adhesions of colon to liver; peritoneum of small intestine cloudy and covered with thin layer of exudate; on section, mucosa congested, thickened, covered with mucus, appearance of a chronic catarrhal enteritis; no ulcers; the wall of the colon thickened throughout its entire length, showed many congested points but no ulcers, mucosa covered with thick layer of mucus; no pigmentation of mucosa; irregular patches of thinning in the mucosa, apparently wholly covered by mucous membrane, probably healed ulcers; appendix plump, wall thickened, lumen patent; peritoneal surface of stomach covered with fresh fibrinopurulent exudate; wall edematous.

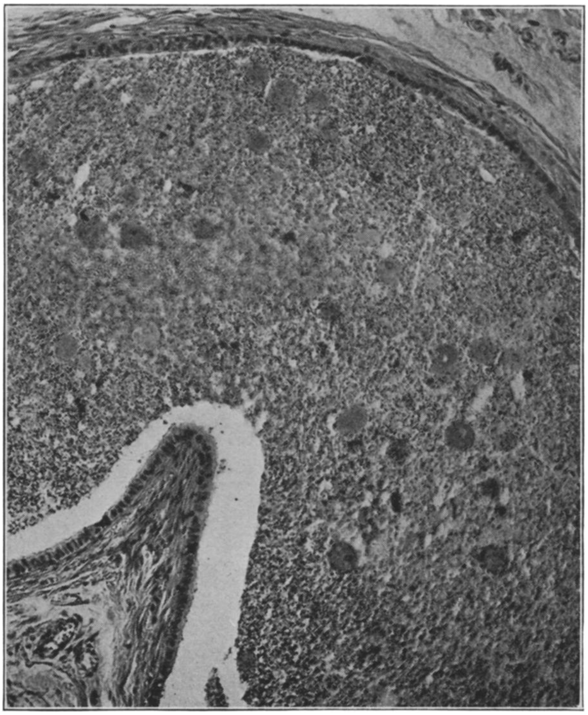

Fig. 4.—Section of body of epididymis showing duct filled with spermatozoa, through which are scattered many amebas. In the semen the amebas are more round and the characteristic annular nucleus and karyosome are clearly seen.

Surface of liver covered with fresh adhesions uniting it to abdominal wall and to incision; liver somewhat enlarged, of firmer consistency, capsule thickened and opaque, particularly on under side, where it shows shallow stellate contractions over the surface; on section, liver is firm, light yellow-brown, lobules small, stroma between lobules increased—early atrophic hepatitis; no abscess; gallbladder dilated, filled with clear pale yellow bile; bile passages patent;

pancreas negative; peripancreatic lymph nodes much enlarged, grayish, translucent, edematous; mesenteric nodes moderately enlarged and edematous.

The suprarenals showed atrophy and excessive lipoidosis; fatty capsules of both kidneys poor in fat; right kidney somewhat larger than left; fibrous capsules slightly adherent, surfaces smooth; small calculus in pelvis of left kidney; both kidneys pale.

Aorta showed numerous patches of fatty change in its intima.

Retroperitoneal lymph nodes and hemal nodes enlarged.

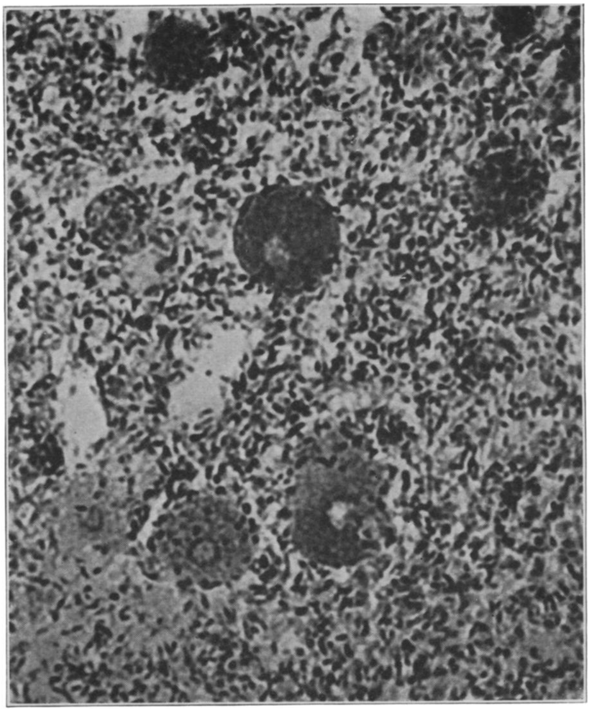

Fig. 5.—Higher power view of portion of field shown in preceding figure; entamoeba histolytica in mass of sperm in epididymis. The characteristics of the nucleus are well shown, as is also the phagocytosis of spermatozoa by them.

Epididymis dilated; spermatocele on left; left testis large, on section showed fibroid patch; right testis smaller and firmer, stroma increased; prostate slightly enlarged; seminal vesicles dilated, full of semen; seminal ducts dilated. The bladder contained purulent urine, mucosa negative.

The microscopic examination of the different organs and tissues revealed:

Heart: Sclerosis of epicardium; fatty infiltration of subepicardial tissue with beginning serous atrophy; simple atrophy, cloudy swelling and fatty degenerative infiltration of heart muscle; early coronary sclerosis; a few small active areas of syphilitic myocarditis; sclerosis of endocardium.

Lungs: Croupous pneumonia, delayed resolution, multiple abscesses and beginning organization; purulent bronchitis; no amebas in abscesses; marked anthracosis.

Tongue: Marked fibroid hypeprplasia of the papillae with atrophy of the lymphoid tissue; chronic syphilitic glossitis.

Aorta: Slight sclerosis of the intima; a few small plasma cell infiltrations around the vasa vasorum; early syphilitic mesaortitis.

Spleen: Marked chronic passive congestion with marked increase of stroma; diffuse fibrosis with atrophy of the lymphoid tissue; sclerosis of artioles; acute fibrinous perisplenitis.

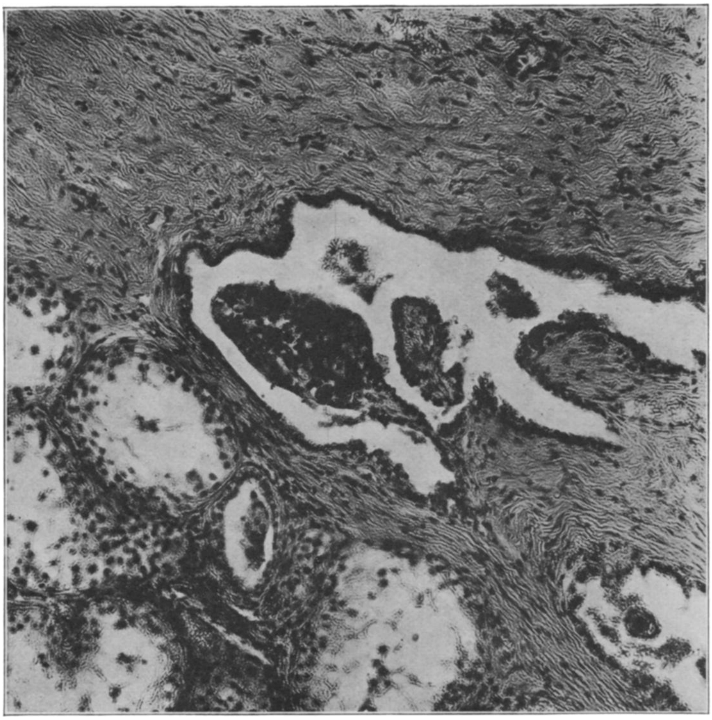

Fig. 6.—Mass of ameba cysts attached in clot to small ulcer or erosion in duct of rete testis.

Liver: Well advanced atrophic cirrhosis; areas of plasma-cell infiltration and proliferation of blood vessels and stroma (syphilitic hepatitis), most marked at periphery of lobules; new formation of bile ducts; acute fibrinopurulent perihepatitis; no abscesses in liver.

Pancreas: Slight fatty atrophy; areas of interstitial pancreatitis (syphilitic); fibrosis of some of the islands; marked dilatation of pancreatic ducts.

Suprarenals: Capsules thickened; atrophy with lipoidosis of the parenchyma; small plasma-cell infiltrations in the medulla.

Kidneys: Slight atrophy and cloudy swelling; marked passive congestion; few casts; many of the tubules dilated; early sclerosis.

Ureters: Dilated; otherwise negative.

Bladder: Negative.

Stomach: Chronic catarrhal gastritis; mucosa atrophic in areas, in others showing a polypoid hypertrophy; no normal gastric glands; acute fibrinopurulent peritonitis.

Small Intestine: Marked chronic catarrhal enteritis; no ulcers; subacute peritonitis.

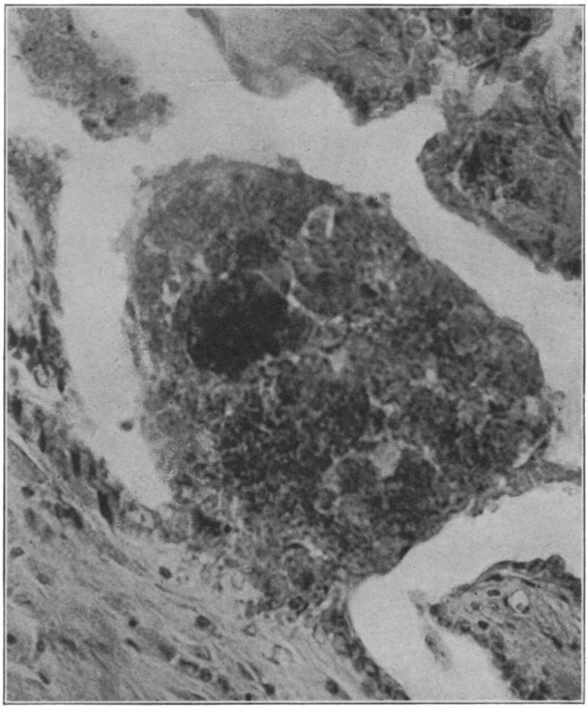

Fig. 7.—Higher power view of blood clot attached to small ulcer in tubule of rete testis, containing Entamoeba histolytica in various stages of development, many adult forms filled with red blood cells. Precystic and cyst forms. The faint granulation of the stroma cells in the lower right hand corner is hemosiderin.

Colon: Severe chronic catarrhal colitis; mucosa atrophic in areas, hypertrophic in others; numerous small healing and healed ulcers with regeneration of epithelium and hyperplastic margins; no amebas found; nearly healed dysentery; fibrosis of all coats.

Appendix: Chronic catarrh.

Mesenteric Lymph Nodes: Chronic lymphadenitis with marked sinus catarrh.

Prostate: Slight glandular hyperplasia and cystic dilatation; no inflammatory changes; no amebas found in any of the gland spaces or ducts.

Seminal Vesicles: Dilated with albuminous fluid containing many spermatozoa; no amebas found.

Vas Deferens: Both seminal ducts were moderately dilated above, more markedly so below. In the lower dilated portions there were pink-staining fibrinous clots of loose texture containing numerous typical amebas of the histolytica type. These clots only partly filled the lumen of the duct and were not attached to the wall; they increased in size toward the epididymis, giving the appearance of floating up into the tube from below.

Epididymes: Both, but particularly the left, showed marked dilatation of the ducts. These were filled in part with masses of spermatozoa through which great numbers of amebas were scattered. In the sperm-filled ducts there was little fibrin, and the amebas were rounder than in the fibrin clots in the vasa. No blood cells were found in the amebas in the semen; but there was marked phagocytosis of spermatozoa by the amebas. On the left side a number of the large dilated ducts in the head of the epididymis contained a heavy albuminous, almost hyaline, precipitate, without spermatozoa or amebas, apparently blind tubules. About the ducts the connective tissue was thickened and the blood vessels were sclerotic, but there was slight active inflammatory reaction. The ductuli efferentes of the lobules of the epididymis and of the mediastinum testis and extending into the rete testis were all dilated but were free of sperm. They contained, however, numerous small fibrin clots, in the meshes of which amebas in various stages of development were present. These clots were either attached at some point to the wall of the duct, or extended into the ducts of the rete where they were attached. At the point of attachment of the clot the epithelium was absent, and the duct wall showed a superficial ulceration. Small hemorrhages in the tissues of the wall of the duct occurred beneath the attachment of the clot and in its neighborhood. The stroma cells were increased in number and size, and contained fine yellowish-brown granules of a pigment giving the iron reaction (hemosiderin). In the clot attached to the lining of the duct amebas in all stages of development were present, many precystic and cystic forms. The adult types showed marked phagocytosis of red blood cells, especially those in the portion of the clot next to the denuded tissue. In many of the clots a layer of amebas lay in direct contact with the connective tissue, and in a few places some of the amebas had penetrated a slight distance into the tissue-spaces. The appearances were those of an actual active erosion of the duct wall by the parasites. Fresh hemorrhages of minute size accompanied this invasion, and the invading amebas showed active phagocytosis of the red blood cells. No phagocytosis of seprmatozoa was seen in the amebas in the rete testis.

Testes: Many seminiferous tubules showed aspermatogenesis with vacuolation of germ cells; other tubules showed active spermatogenesis. The stroma was increased and edematous. Small patches of fibroid atrophy (syphilitic) occurred, more marked in the left testis than in the right. A few seminiferous tubules near the rete were dilated, filled with sperm, and contained amebas mixed with spermatozoa. These amebas showed phagocytosis of the sperm, as in the epididymis. No red cells were distinguishable in these amebas. There was no reaction, and no pigmentation around these tubules.

The amebas found in the testes corresponded in every way to those previously found in the stools of the patient when first seen, and were identified as Entamoeba histolytica. The size of the organisms, the character of the nucleus, its annular appearance, the characteristic central karyosome with halo, eccentric position of the nucleus, the marked phagocytosis of spermatozoa and red blood cells, the production of slight but definite tissue lesions, and the character of the precystic and cystic forms—all of these points establish the diagnosis beyond doubt. In the dilated duct of the epididymis many degenerating forms were present, as well as precystic and cystic forms. In the clots the contraction of the fibrin reticulum caused more or less distortion during fixation, the organisms being slightly compressed or contracted into a more elliptical form.

The complete pathologic diagnosis was: Unresolved croupous pneumonia, with early abscess-formation and organization; purulent bronchitis; early atrophic cirrhosis; chronic passive congestion of spleen with fibrosis; healed chronic dysentery (amebic); metastasis of Entamoeba histolytica to epididymes and testes with local lesions; latent syphilis (leptomeningitis, myocarditis, hepatitis, pancreatitis, mesaortitis, orchitis, etc.); early sclerosis; atrophy, parenchymatous degeneration and passive congestion of all organs; recent laparotomy; tattoo.

This case, therefore, presents the unique occurrence of the metastasis of Entamoeba histolytica to the epididymes and testes with definite, though slight, local lesions in these organs, in a patient affected for many years with amebic dysentery, at the time of death nearly completely healed, with disappearance of amebas from the stools. It is the first recorded instance of such a localization of Entamoeba histolytica, and presents additional evidence of the mildly pathogenic character of this parasite, in the slight tissue destruction caused by it and its phagocytosis of red blood cells and spermatozoa. A point of some interest is the localization of the small lesions in the rete testes and tubuli efferentes, with long streaming clots extending upward into the epididymis, the amebas being held within these clots. In the dilated semen-filled portions of the epididymis the organisms were found in greater numbers and free in the semen. Their commensal character is shown by the phagocytosis of red blood cells in the clots, and by that of spermatozoa in the semen particularly; that is, they show the same tendency in the semen to feed on substances contained in it as they do on the substances in the intestinal contents.